REVIEW

Maintenance of endemicity in urban environments: a hypothesis linking risk, network structure and geography

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In industrialised countries, a rapid epidemic phase of HIV transmission has largely given way to more moderated endemic transmission. The dynamics of endemic transmission may differ substantially from those generating epidemic spread. We hypothesise that three elements play an important role in maintaining endemicity in high prevalence urban environments. First, persons are likely to be subject to multiple risks from multiple sources rather than engaging in a single, hierarchically classified, risk behaviour. Second, the network structure in these environments may include a substrate of "fixed" factors (a large connected component, a characteristic degree distribution and small world phenomenon) upon which is superimposed a number of variable factors (transitivity, assortativity) that determine the level of prevalence. Third, the geographic range of persons in these milieux is constricted, making it likely that new partners will already be connected. The confluence of these three factors assures the ongoing risk bombardment needed for maintenance of endemicity. Further empirical and theoretical analysis will be required in order to validate this hypothesis.

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In the US, the epidemic form of HIV during the 1980s and early 1990s was dominated by the most infectious routes of transmission: transfusion, sharing of infected needles and injection equipment, and unprotected anal intercourse between men.[1–3] In the current endemic state of HIV transmission, the last two risks are still dominant, but have been modified by changes in behaviour, by the influence of non-injecting drug use and by social arrangements within communities at risk. Penile–vaginal sex carries a small probability of transmission in most estimates,[4] but may have an important role in communities where drug use, drug injection, penile–anal sex between men and bisexuality are common. The endemic persistence (and, in fact, recrudescence in some areas) of HIV may be predicated on a variety of direct channels for transmission (sharing of infected needles and equipment, unprotected penile–anal sex among partners of the same and opposite sexes, penile–vaginal or oral–anal sex), coupled with exchange of sex for drugs or money, and the amplifying presence of other infections (sexually transmitted infections and blood-borne infections). Multiple channels, multiply delivered by multiple partners, may be necessary for the continued endemicity of HIV, other sexually transmitted infections and blood-borne infections.[5] Such a picture adds more complexity to the traditional hierarchical view of HIV risks, and alters the approaches for intervention.

Robins and Pattison[6] pointed out that for a social network, "the only intentionality in the system is at the level of the actor, that is, locally". Morris[7] suggested that local rules (meaning choices made by people at risk or factors that influence such choices) will generate the global properties of networks. She notes, for example, that the sequencing of sexual partners (concurrency *v* serial monogamy) and attribute mixing seem to be major determinants of network configuration. Global properties arise from four local choices made by people at risk: the number of partners used for sex and drug exchange, the characteristics of people that make them suitable partners, the temporal sequencing of these partners (serial or simultaneous), and the types and frequency of specific risky acts. The specific mix of such choices by network members will give rise to the global network configuration. In the setting of urban endemic transmission (and possibly elsewhere), I propose that local choices are strongly influenced by the availability of partners and by personal mobility. It follows that geographical considerations are important determinants of prevalence and infectivity.

HYPOTHESIS

The model for endemic transmission emerging from these considerations (fig 1) is that local choices in a high-density urban setting will generate compound risk and also critical network characteristics. In addition, in the inner-city environment, the group at risk shows remarkable compactness and cohesion, so that even people at considerable social distance (eg, six or more steps apart) remain within the same geographical space. This spatial proximity suggests an increased probability that selection of new partners will be made between people who are already connected to each other and are part of the network at risk. The geographical compactness thus acts as a self-reinforcing mechanism for continuing endemicity. In the following sections, I present briefly some of the evidence that supports these contentions.

ROLE OF COMPOUND RISK

In establishing the hierarchical classification of risk for HIV ("Arbitrarily, homosexual or bisexual men were placed first in the hierarchy whether or not they had other risk factors", Jaffe *et al*,[3] p 341),

Abbreviations: IDU, injecting drug user; MSM, men who have sex with men

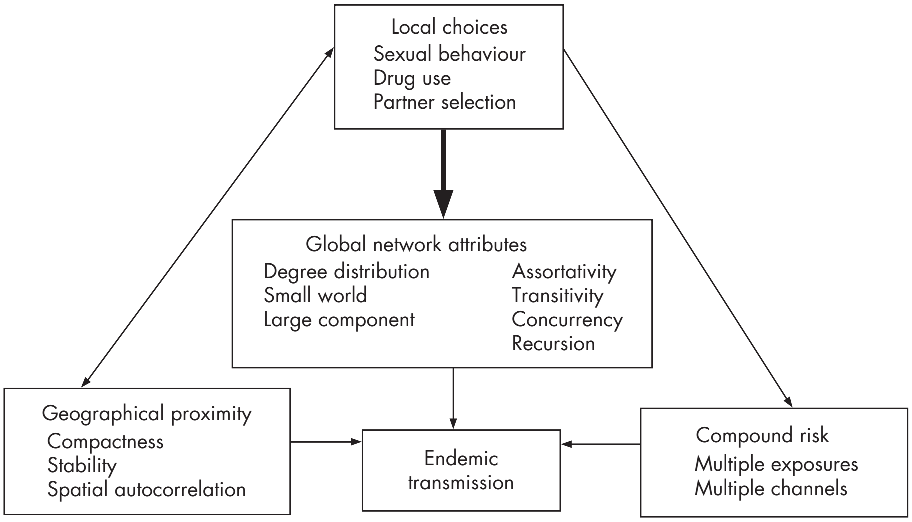

Figure 1 Proposed model for endemic transmission in urban inner-city areas.

Jaffe *et al* also noted that the groups were not mutually exclusive: 81 of the first 1000 cases of AIDS were injecting drug users (IDUs)/men who have sex with men (MSM); thus, 35% (81/235) of the IDUs in this group were also MSM. The traditional hierarchical classification of HIV/AIDS risk does include several assessments of joint risk, with the recent observation that IDUs/MSM maintain a high burden of risk.[8] The contribution of IDUs/MSM to overall HIV/AIDS infection has decreased from 8% in 1990 to 5% in 1998[9]; however, 22% of male IDUs reported nationally with HIV/AIDS also admit to having sex with men. Despite the joint risk of HIV acquisition for IDU/MSM's being a recognised feature of the AIDS landscape since the inception of the epidemic, it has received relatively little attention. The relatively low frequency of joint risk in the earlier years may have been overshadowed by the obvious primacy of anal intercourse and needle sharing as independent risks. A modest number of studies (table 1)[10–33] has pointed out that the combination of IDUs and MSM consistently poses the greatest hazard for HIV acquisition, with a relative risk odds ratio (OR) (or rate ratio) between 4 and 25, and HIV prevalence and incidence consistently 2–3 times that in male IDUs who do not have sex with men. In some studies, the prevalence of MSM among IDUs is ⩾10%, although in most studies cited in table 1, the prevalence was lower. The overall impression was best summarised by Deren *et al*[22] in their multisite evaluation of IDU risk: "…being a gay drug user is the best predictor of being seropositive across all communities studied … particularly so in low-IDU seroprevalence sites". Although not stated explicitly, the impression from these studies is that IDUs/MSM may have a role in transmission that is out of proportion to their numbers.

Table 1 Risks for HIV associated with occurrence of injection drug use among men who have sex with men

First author, year	Sample size	Observations
Kottiri,[10] 2002	662 IDUs	IDU/MSM prev 1.7%; OR for HIV+ 4.02
Bull,[11] 2002	100 IDUs/MSM	45% HIV+; documentation of risk behaviour
Maslow,[12] 2002	NA	Decline of prev in MSM/IDU from 60.5% to 43.8%, 10 years
Nelson,[13] 2002	1846 IDUs	Seroconv: IDU/hetero, 3.05; IDU/MSM, 5.91; OR changed (6.95, 7.95, 7.03) over a 10-year interval
Rothenberg,[14] 2002	358 person-years	For IDUs: up to 22% were MSM; up to 23% had RAI; 20% of women had RAI (see text)
Kral,[15] 2001	1192 IDU	Among 31 seroconverters 45% were MSM *v* 9% non-converters
Diaz,[16] 2001	156 Latino Dus	7% MSM; HIV+ non-MSM 18% *v* hetero 5%
Bruneau,[17] 2001	2741 IDUs	Prev of HIV: IDU/hetero, 10.4%; IDUs/MSM 27.2%
Strathdee,[18] 2001	1874 IDUs	69 IDUs/MSM; seroconv: IDUs/hetero, 3.01 per 100 person-years; IDUs/MSM, 10.4 per 100 person-years; rate ratio 4.04
Rothenberg,[19] 2001	228 person-years	Overall prev 13.1%; IDUs/MSM, 40%; highest OR associated with MSM, 5.1
Suligoi,[20] 1999	1950 IDUs	Incidence: IDUs/MSM 13.8 per 100 person-years; IDU/non-MSM 4.6 per 100 person-years
Des Jarlais,[21] 1999	5119 IDUs	Overall, 7% IDU also MSM; of IDUs/non-MSM, 37% HIV+, of IDUs/MSM, 49% HIV+
Deren,[22] 1997	3002 IDUs	1.2% IDUs/MSM; 2.4% IDUs/bisexual; 96.4% IDUs/hetero; OR for HIV+ among IDUs/MSM 17.3–24.7 (different models)
Friedman,[23 24] 1997	765 IDUs	IDUs/MSM prev 3%; IDUs/WSW prev 16% IDUs/MSM HIV+, 67%; IDUs/non-MSM HIV+, 39%
Sorvillo,[25] 1996	1857 HIV+	OR for recent infection: women, 3.4; black, 1.6; IDUs/MSM, 2.4
Friedman,[26] 1995	6882 IDUs/15 cities	High-prev cities: 1.8% IDUs were MSM; low-prev cities: 2.5% IDUs were MSM; RR for seroconv 3.9
Lewis,[27] 1994	396 IDUs	Risk prev: MSM, 11.6%; bisexual, 12.5%; hetero, 76%; HIV+: MSM, 54%; bisexual, 24%; hetero, 9%
Jose,[28] 1993	660 IDUs	OR 3.58 for MSM and HIV+ (highest of all variables tested)
Siegal,[29] 1991	855 IDUs	4% IDUs were MSM; 9.1% IDUs/MSM were HIV+ *v* 1.3% overall OR for HIV+ by IDUs/MSM 11.2
Ross,[30] 1991	880 male IDUs	13.3% bisexual; 6% homo HIV+: hetero, 3.2%; bisexual, 12.1%; homo, 36%
Williams,[31] 1990	131 IDUs	MSM, 15%; >50% had sex with non-IDUs
Marmor,[32] 1987	214 IDUs	IDUs/MSM, 68% HIV+; IDUs/non-MSM, 46% HIV+
Smith,[33] 2004	206 MSM	—

Hetero, heterosexual; HIV+, HIV positive; homo, homosexual; IDU, injecting drug user; MSM, men who have sex with men; NA, not available; non-MSM, men who do not have sex with men; prev, prevalence; RAI, receptive anal intercourse; seroconv, seroconversion; WSW, women who have sex with women.

Table 2 Characteristics of 15 networks in which transmission of HIV and sexually transmitted diseases has been studied

Network attribute	Defining feature	Results from 15 network studies
Substrate for transmission		
Degree distribution	A small number of people with a large number of partners, giving the distribution a long ("fat") tail to the right, possibly scale free in some instances	Exponent associated with calculation of a power law curve for each study: range 1.6–4.1; mean 2.0*
Component distribution	A very large component involving most people in the network; the second largest component is smaller by ⩾1 orders of magnitude	Among larger studies, ratio of largest to next largest component varied from 40:1 to 100:1; more variable among smaller studies (from a single component to a 1:1 ratio), in part because of sampling differences
Average distances between people (small-world phenomenon)†	Short geodesics (smallest distances between nodes) and short diameter (the longest shortest distance is short); geodesics increase with the log of network size (or slower)	The R^2 for correlation between mean geodesic (corrected for network size) and log of number in networks is 0.77
Variable factors		
Transitivity (clustering)	The proportion of triads (three connected people) that are "closed" —that is, that forms a triangle	Clustering is absent, by definition, in heterosexual relationships; the clustering coefficient varied from 0 (only heterosexual contact) to 0.33 in one study on IDUs†
Concurrency‡	The number of concurrent relationships per contact, where concurrent is defined as activity with two other people over a given time interval	Concurrency ranged from 1.4 to 10.8
Assortativity§	The extent to which people with similar characteristics (age, ethnicity and degree) associate with each other in preference to associating with dissimilar people	Overall (including both sexes and needle contacts), age assortativity ranged from 0.20 to 0.44; ethnic assortativity from 0.13 to 0.77; and degree assortativity from 0.15 to 0.52
Recursion¶	The proportional difference between the actual number of people in a network and the number that there would be if all people named in egocentric interviews were different	Recursion ranged from 14.3% to 57.6% in these studies

IDU, injecting drug user.
*Calculated using Newman's[36] method. Alternative methods, based on maximum likelihood, may provide a better estimate of the power law exponent.[37]
†Short distances between people characterise random networks and small-world networks. The small-world phenomenon is observed when short distances are coupled with local clustering, generated by nodes with high connectivity and "short cuts".[38 39]
‡Calculated using Morris and Kretzchmar's[42] method.
§Calculated using Newman's[40] method. This approach provides a single summary statistic for the extent to which assortative mixing occurs on the basis of a given trait. A more comprehensive approach, using a log–linear approach, has been developed by Morris.[41]
¶The amount of recursion is based to some extent on study design,[19] but it can still serve as a rapid assessment of the amount of internal structure in a network.

Lack of appreciation of the role of joint risk—and possibly of multiple risks as well—may result from the traditional categorisation of people as IDUs or MSM or both, rather than more detailed attention to actual risky acts performed. In a study on urban dwellers in Atlanta at risk for HIV because of their drug use and sexual activity (without a priori categorisation), we noted that only 6.9% of men stated that they had a same-sex sexual orientation, but 28.3% reported practising insertive anal intercourse with men. In parallel, 19% of women had a female sexual orientation and one third reported that they had had sex with women. Although women were often involved in economic exchange of drugs or money for sex (71.2%), about one third of men were also involved in such exchanges. Of the 292 men and women in this group, 25% had shared needles or drugs in the previous 3 months. Moreover, the frequency of joint risk varied by study site: 32.8% of relationships at one site involved both needle sharing and drug use compared with 3.4% at another site.[19] In a follow-up study of the same population, Rothenberg *et al*[5] attempted to combine elements of joint risk in a four-digit binary risk indicator.[5] Detailed examination of this indicator in the context of actual networks highlighted the primacy of drug-using MSM for generating a new case of HIV.

The risk pattern observed in this Atlanta study was also seen in a subsequent examination of 358 people recruited in a clinic and in the community.[14] Within the community HIV-positive group, 22% of men who injected drugs reported a male sexual orientation and 28% reported recent receptive anal intercourse, as did 20% of women recruited from the community. That study considered several factors (in addition to behaviour and network configuration), and noted that participants, especially community-recruited HIV-positive people, had high levels of social stress (also measured as a binary number that included imprisonment, homelessness and unemployment) and had profiles for psychological stress (as measured by the Brief Symptom Inventory) that were equivalent to those for an inpatient psychiatric population.

These studies in Atlanta and others shown in table 1 highlight the multifactorial nature of risk, including, but not limited to, the interaction between IDUs and MSM. The importance of joint risk in transmission is supported (although not proved) by Bernouilli models of multiple "hits",[4 34] wherein the frequency and variety of exposures increase the cumulative probability of transmission. As the AIDS epidemic continues to evolve, with an increasing pattern of endemic entrenchment in inner-city minority communities, the joint occurrence of risks will probably have a larger role in maintaining such endemicity and effective interventions will depend on a broader understanding of the multifactorial nature of risk.

THE NETWORK SUBSTRATE FOR DISEASE TRANSMISSION

In an ongoing analysis of 15 completed network studies,[35] we examined the characteristics of networks wherein HIV and sexually transmitted diseases were transmitted. One picture emerging from these data is that actively transmitting networks seem to share a substrate of common characteristics (table 2).[36–41] First, they have a degree distribution with a long ("fat") tail to the right, signifying the presence of a small number of people who have a large number of contacts. Although it is unclear that these networks are scale free (with a power law coefficient between 2 and 3), they do have highly active nodes that serve as foci for clustering and distribution of disease (in a general sense, clustering refers to heightened interconnectivity among nodes, but more specifically refers to the frequency of "closed triangles"—ie, the proportion of triads that are completely connected). Second, they are characterised by short pathways (ie, the mean geodesic, or the shortest distance between two nodes, increases proportionally to the logarithm of the number of people in the network, rather than proportionally to the number itself). Taken together, short pathways and local clustering define the small-world phenomenon, which transmitting networks seem to display. Third, the larger networks in this group all have a single, large connected component; the second largest component is smaller by ⩾1 orders of magnitude. These three characteristics produce the contiguity and interaction that seem to be necessary for disease propagation.

The amount of propagation is, however, variable, and this may be the result of variability both in this substrate and in other network characteristics. Transitivity (or clustering), for example, does not occur in purely heterosexual networks. It can occur in a setting in which needles are shared, or among MSM (or women who have sex with women, although it is generally accepted that the potential for transmission in this setting is substantially lower than in the other settings mentioned). The nature of the risks in a network leads to markedly different levels of clustering (the very active nodes, if heterosexual, will create short paths but no clustering). Concurrency, or the presence of two partners in a defined time frame, may also be variable, and concurrency, it has been argued, is a key structural factor in raising the probability of propagation of endemic diseases.[42–44]

The extent to which people engage with those who share their characteristics (assortative mixing) or with others who are not like them (disassortative mixing) will have an important effect on transmission. For example, young homosexual men face a different prevalence if they choose partners who are peers or partners who are older. The precise effect of assortativity may differ in different settings, however, and may be hard to predict a priori. As shown in table 2, assortativity by age, ethnicity or degree is highly variable, and its individual and joint effects are likely to be important determinants of incidence and prevalence.

Several of these critical network characteristics are captured, albeit only in summary fashion, by the concept of recursion. If in a set of egocentric interviews, none of the respondents is connected directly or through his or her contacts to any other respondent, the total number of people named will be the sum of respondents and their contacts. If, however, such interviews result in the naming of substantially fewer people (as respondents name each other and name some of the same contacts), there must be considerable interconnection among them. Recursion is the proportional reduction in the number of different people named compared with the number there would be if all people named in the interviews were different. High recursion implies the presence of some nodes with high degree, a large component, short pathways, considerable clustering (depending on the type of risk) and substantial concurrency. It does not, however, capture any of the detail that these measures contain, but may be thought of as a ''quick and dirty'' measure of connectivity. In the studies examined (table 2), recursion varies considerably, and in step with the other variable characteristics. Clearly, a small amount of recursion need not be associated with any of the network effects described, but such an association is likely to increase with the increasing proportion of people who name those who are already named.

Smith *et al*,[33] who conducted egocentric interviews on 206 MSM in an urban environment, gave some evidence against this construct. They found that injecting drug use increases the occurrence of anal sex in this group (table 1), but that network density—which, like recursion, is an overall measure of interaction—was inversely related to the number of oral or anal network partners. Although the authors assembled their group through chain link referral, they did not present sociometric information that might have offered more detail about the network structure created by higher egocentric density.

GEOGRAPHICAL DETERMINANTS

The ability to meld geographical information with a variety of other population and individual characteristics has improved the understanding of environmental, cultural and social influences.[45] Geocoding—providing coordinates to places, events, geographical features or people—permits the measurement of distances and depiction of the spatial relationships among such objects. Placement of these objects in defined boundaries permits the calculation of areal rates, often depicted as choropleths (maps whose areal shading has quantitative meaning). These approaches—features of the larger field of geographical information systems—are now used extensively in public health and descriptive epidemiology.[46]

The analytic framework for geographical analysis is often defined by the structure of the data. Anselin[47] discusses two complementary data methods, geostatistical and lattice, that differ in the way they capture spatial correlation between observations. Geostatistical approaches use a distance metric where correlation between values (attributes) declines with distance. This approach requires geocoding of people using several alternative sites (domicile, places of aggregation, centroid of a range of places, etc) and calculating the distances between people as a function of their characteristics. As an example, using exploratory spatial data analysis,[47] the distribution of distances between dyads that include IDUs/MSM (median, fourth spread, whiskers, outliers) can be compared with the distribution for those who only inject drugs. The extent of spatial similarity between pairs is often visualised using the variogram, a plot of the variance of differences in outcomes (eg, disease status) between people in a dyad to the distance between their respective locations.[48]

In contrast with distance-based geostatistical methods, lattice approaches apply to aggregate data from small areas (eg, census tracts), and describe spatial correlation using spatial weights. For a particular region, the value of an attribute can be compared with a weighted average of the values of its neighbours. This comparison may be depicted as a spatially lagged scatter plot (Moran scatter plot or correlogram), for which a 45° linear association indicates strong spatial autocorrelation. A typical global statistic is Moran's I,[49] which measures the correlation of an area with its neighbours, usually given as

$$I(d) = \sum_{i}^{n}\sum_{j}^{n} w_{ij}(x_i - \bar{x})(x_j - \bar{x}) \Big/ S^2 \sum_{i}^{n}\sum_{j}^{n} w_{ij}$$

where

$$S^2 = \frac{1}{n}\sum_{i}^{n}(x_i - \bar{x})^2$$

x_i is the observed value at location i and $\bar{x}$ is the average of the x_i over n locations.[50] The spatial weights, w_{ij}, are a defined measure of contiguity for the regions I and j.

This type of formulation can be adapted to incorporate network information directly. If the members of a connected component are placed on a map in real space, retaining the network links, and a circle of radius r is drawn about any member, autocorrelation of that member with the people within the radius can be calculated for a variable of interest (the x_i's), using the reciprocal of the geodesic (the shortest network path distance) from that member to each of the members included within the radius as the weight. Repetition

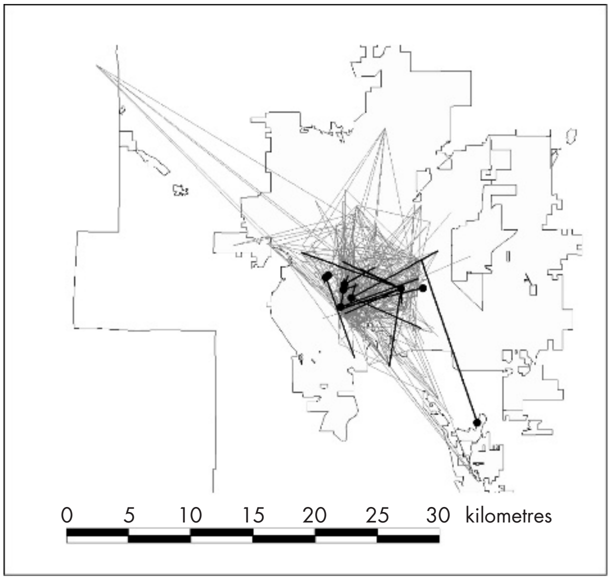

Figure 2 Network of connected people in Colorado Springs who are at risk for HIV transmission. Connections are showed in real space. The dots are people with HIV and the heavy lines are their direct connections to others. Several figures, similar but not identical to this one, have been previously published.[28]

of this process with increasing radii to encompass everyone in the network gives the Moran scatter plot (the values for x_i plotted against the values for his or her neighbours). If this process is performed for each network member, a statistic (I(d), or the regression coefficient) can be calculated for use in multivariable analysis to determine the effect of spatial autocorrelation on prevalence or acquisition of sexually transmitted infections/HIV/blood-borne infections. Used in this way, measures of spatial autocorrelation are the geographical equivalents of assortativity measures.

To date, there has been little formal incorporation of geographical attributes into network analysis. Muth *et al*[51] used geographical information from the Colorado Springs Study to show that people enrolled and not enrolled in the study were similar in their geographical distribution, thus reinforcing Tobler's[52] hypothesis that people will be similar to those near them. The authors proposed this technique,[51] which involved the use of a rotating box plot, as a method to confirm the representativeness of a study population. Zenilman *et al*[53] measured the distances between people with gonorrhoea and their partners. They showed considerably smaller distances between dyads within core areas of Baltimore than those within non-core areas, reinforcing the importance of local neighbourhood and geographical compactness in the dynamics of gonorrhoea transmission. Jennings *et al*,[54] using reported case data from Baltimore, confirmed the geographical clustering, although without explicit network information.

We recently analysed the relationship between social distance (the geodesic between people in a connected component) and actual geographical distance.[55] In these data from the Colorado Springs Study, we selected a subgroup of 348 respondents who were also named as contacts.[56–58] These people formed a connected component for which the social distance (ie, the geodesic or shortest path between them) and the geographical distance could be compared directly. The geodesic varied from 1 to 14 (making 14 the "diameter" of the network). The actual distance varied from several hundred metres to >20 km. Dyads with a geodesic of $\leqslant$8 steps—which constituted 96% of the dyads in this analysis—had a median distance between their members of 6.7 km. The study showed the compactness of a large group of connected people, whose distance from each other varied by risk group and type of relationship. People who share sexual and drug risks, and HIV-positve people and their contacts, were closest. Prostitutes and their paying partners were more distant. About half of the dyads in this study were $\leqslant$4 km apart. Of the people in the group 57% were 1–6 steps apart and 0–8 km from each other. The mean distance between connected people in this network was 5.3 km. By contrast, we estimated that the mean distance between people in the general population of Colorado Springs was 14.3 km. A similar pattern was found when social distance was measured by the strength of the relationship. The placement of this network in real space (fig 2) provides a graphic depiction of the role contiguity may have in maintaining endemic transmission.

HYPOTHESIS REVISITED

The hypothesis (fig 1) is by no means proved. The data on compound risk, network structure and geographical proximity presented here are derived from multiple sources. Although the joint risk of injecting drug use and sex between men has been shown in settings of heightened HIV endemicity (table 1), the more general characteristic of multiple routes with multiple exposures needs further documentation. Qualitative relationships between network structure and transmission have been suggested, but a firmer quantitative footing is required, and is hindered by the relative scarcity of full-bore empirical network studies. Such relationships will probably be shown by the modelling and simulation efforts that are under way. The relationship between social and geographical distance is now suggested by several studies, but requires more thorough evaluation. Clearly, a single study that involves all three elements and other potential confounders will be of value in assessing their joint interrelationship (one such study is now in progress). If substantiated, this hypothesis may have some explanatory value for understanding transmission dynamics.

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